Document Type: C

RATH GENES AND POLYPEPTIDES AND METHODS FOR THE TREATMENT AND DIAGNOSIS OF IMMUNE DISORDERS; DETECTING NUCLEIC ACID INVOLVED IN G PROTEIN MEDIATED

SIGNAL TRANSDUCTION IN A T HELPER CELL SAMPLE

Inventors: Gimeno Carlos J (US); Levinson Douglas Adam (US)

Assignee: Millennium Pharmaceuticals Inc

Assignee Code: 41994

Attorney, Agent or Firm: Pennie & Edmonds LLP Publication (No, Kind, Date), Applic (No, Date):

US 6146827 A 20001114 US 97949004 19971010

Calculated Expiration: 20161004

Cont.-in-part Pub(No), Applic(No, Date): US 5846780

96726228 19961004

Division Pub(No), Applic(No, Date): US 6020142

US 97870815

US

19970606

Priority Applic(No,Date): US 97949004 19971010; US 96726228

19961004; US 97870815 19970606

Abstract: The present invention relates, first, to the identification of novel nucleic acid molecules, termed RATH genes and RATH gene products encoded by such nucleic acid molecules, or degenerate variants thereof, that participate in the regulation, control and/or modulation of G-protein-mediated signal transduction involved in T cell activation, including, but not limited to T helper (TH) cell and TH cell subpopulation activation. Specifically, the nucleic acid molecules of the present invention include the genes corresponding to the mammalian RATH genes, including the RATH1. \*\*\*1\*\*\* genes. Sequence analysis indicates that the RATH genes are novel genes belonging to the RGS ("regulator of Gprotein signalling") gene family, a gene family which encodes gene products involved in G-protein-mediated signal transduction.

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Publication (No,Kind,Date), Applic (No,Date):
... ***20001114***
```

Abstract: ...the present invention include the genes corresponding to the mammalian RATH genes, including the RATH1. \*\*\*1\*\*\* genes. Sequence analysis indicates that the RATH genes are novel genes belonging to the RGS...

Exemplary Claim:

#### DRAWING

 $\mbox{***1***}$  . A method for detecting a RATH nucleic acid molecule in a T helper cell sample...

```
...encoded by the cDNA clone of ATCC Accession No. 98116 under conditions comprising incubation at ***65*** degree(s) C. in 0.5 M NaHPO4, ***7*** % ***SDS*** , ***1*** mM EDTA followed by washing in 0.1XSSC/0. ***1*** % SDS
```

at 68 degree(s) C.

Non-exemplary Claims:

2. The method of claim \*\*\*1\*\*\* , wherein the reagent detects an mRNA molecule...

```
...encoded by the cDNA clone of ATCC Accession No. 98116 under conditions comprising incubation at ***65*** degree(s) C. in 0.5 M NaHPO4, ***7*** % ***SDS*** , ***1*** mM EDTA followed by washing in 0.1XSSC/0. ***1*** % SDS
```

at 68 degree(s) C...

...encoded by the cDNA clone of ATCC Accession No. 98116 under conditions comprising incubation at \*\*\*65\*\*\* degree(s) C. in 0.5 M NaHPO4, \*\*\*7\*\*\* % \*\*\*SDS\*\*\* , \*\*\*1\*\*\* mM EDTA followed by washing in 0.1XSSC/0. \*\*\*1\*\*\* %

at 68 degree(s) C...

```
...nucleic acid molecule with nuclcic acid of the cell sample under conditions comprising incubation at ***65*** degree(s) C. in 0.5 M NaHPO4, 7% SDS, 1 mM EDTA followed by washing in: (i) 0.1XSSC/0. ***1*** % SDS at 68 degree(s) C., or (ii) 0.2XSSC/0. ***1*** % SDS at 42 degree(s) C.; and (b) detecting, by hybridization of the probe to...
```

- ...molecule of the cell sample under highly stringent conditions comprising washing in 6XSSC/0.05% \*\*\*sodium\*\*\* \*\*\*pyrophosphate\*\*\* at a wash temperature of 37 degree(s), 48 degree(s), 55 degree(s), or9. The method of claim 1 or 3, wherein the RATH nucleic acid molecule comprises a nucleotide sequence that encodes the...
- ...9, wherein the RATH nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3 or the cDNA clone of ATCC Accession No. 98116...
- ...11. The method of claim \*\*\*1\*\*\* , 3 or 5, wherein the RATH nucleic acid molecule comprises a nucleotide sequence that encodes...
- ...15. The method of claim \*\*\*1\*\*\* or 3, wherein the RATH nucleic acid molecule comprises a nucleotide sequence that hybridizes to...
- ...encoded by the cDNA clone of ATCC Accession No. 98116 under conditions comprising incubation at \*\*\*65\*\*\* degree(s) C. in 0.5 M NaHPO4, \*\*\*7\*\*\* % \*\*\*SDS\*\*\* , \*\*\*1\*\*\* mM EDTA followed by washing in 0.1XSSC/0. \*\*\*1\*\*\* % SDS

at 68 degree(s) C...

...16. The method of claim \*\*\*1\*\*\* or 3, wherein the T helper cell sample comprises a TH1 cell sample.

11/3,K,AB/3 (Item 3 from file: 340) DIALOG(R)File 340:CLAIMS(R)/US Patent (c) 2007 IFI/CLAIMS(R). All rts. reserv.

Dialog Acc No: 2974655 IFI Acc No: 9813551

IFI Publication Control No: 9813551

Document Type: C

PHOSPHOLIPASE D GENE ORIGINATED FROM PLANT; GENES AND CLONING DNA WITH

NUCLEOTIDE SEQUENCES AND HYBRIDS

Inventors: Morioka Shinji (JP); Ueki Jun (JP)

Assignee: Japan Tobacco Inc JP

Assignee Code: 43797

Attorney, Agent or Firm: Birch, Stewart, Kolasch & Birch LLP

Publication (No, Kind, Date), Applic (No, Date):

US 5747327 A 19980505 US 95446794 19950726

Calculated Expiration: 20150505

(Cited in 005 later patents)

Internat. Convention Pub(No,Date), Applic(No,Date): WO 9509234

19950406 WO 94JP1627 19940930

Section 371: 19950726 Section 102(e):19950726

Priority Applic(No, Date): JP 93267884 19930930

Abstract: A cloned DNA encoding phospholipase D originated from a plant and a cloned DNA which regulates expression of phospholipase D gene originated from a plant are disclosed.

Publication (No, Kind, Date), Applic (No, Date):

- . \*\*\*19980505\*\*\*
- ...Internat. Convention Pub(No,Date), Applic(No,Date): \*\*\*19950406\*\*\*

### Exemplary Claim:

- \*\*\*1\*\*\* . A cloned DNA which encodes phospholipase D originated from a plant, wherein said DNA comprises...
- ...nucleotide sequence selected from the group consisting of nucleotides 182-2617 of SEQ ID NO:1 and nucleotides 107-2542 of SEQ ID NO:3 or a sequence complementary thereto or...
- ...to said cloned DNA or said complementary sequence in a hybridization solution containing 0.5M \*\*\*sodium\*\*\* \*\*\*phosphate\*\*\* buffer, pH 7.2, containing 7% SDS, 1 mM EDTA and 100 mg/ml of salmon sperm DNA at \*\*\*65\*\*\* \* C. for 16 hours and washing twice at \*\*\*65\*\*\* \* C. for twenty minutes in a washing solution containing 0.5 X SSC and 0.

  \*\*\*1\*\*\* % SDS.

# Non-exemplary Claims:

. . .

- 2. The DNA according to claim \*\*\*1\*\*\* , which encodes phospholipase D originated from a monocotyledonous plant...
- ...DNA according to claim 3, which has a nucleotide sequence shown in SEQ ID NO. \*\*\*1\*\*\* or has the same nucleotide sequence as shown in SEQ ID NO. \*\*\*1\*\*\* except that one or more nucleotides are added, deleted or substituted, said nucleotide sequence encodes...
- ...DNA according to claim 7, which has a nucleotide sequence shown in SEQ ID NO. \*\*\*1\*\*\* .
- ...sequence from 182th to 2617th nucleotide in the nucleotide sequence shown in SEQ ID NO. \*\*\*1\*\*\* .
- ...DNA which has a nucleotide sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 3 and SEQ ID NO: 5 or a sequence complementary thereto or...
- ...to said cloned DNA or said complementary sequence in a hybridization solution containing 0.5M \*\*\*sodium\*\*\* \*\*\*phosphate\*\*\* buffer, pH 7.2, containing 7% SDS, 1 mM EDTA and 100 Mu g/ml of salmon sperm DNA at 45\* C. or \*\*\*65\*\*\* \* C. for 16 hours and washing twice at 45\* C. or 650\* C. for twenty...
- ...mM sodium citrate or in a washing solution containing 0.5 X SSC containing 0. \*\*\*1\*\*\* % SDS...
- ...said DNA has a nucleotide sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 3 and SEQ ID NO: 5 or wherein said DNA specifically hybridizes to said antisense sequence in a hybridization solution containing 0.5M \*\*\*sodium\*\*\* \*\*\*phosphate\*\*\* buffer, pH 7.2,

11/3,K,AB/1 (Item 1 from file: 340) DIALOG(R) File 340: CLAIMS(R) /US Patent (c) 2007 IFI/CLAIMS(R). All rts. reserv.

Dialog Acc No: 3736646 IFI Acc No: 0229010

IFI Publication Control No: 0229010

Document Type: C

LIPID KINASE; ISOLATED NUCLEIC ACID COMPRISING NUCLEOTIDE SEQUENCE THAT ENCODES HUMAN PI3K-C2-ALPHA, A PHOSPHOINOSITIDE LIPID KINASE, HAVING SPECIFIED AMINO ACID SEQUENCE

Inventors: Domin Jan (GB); Warerfield Michael Derek (GB)

Assignee: Ludwig Institute for Cancer Research CH

Assignee Code: 25199

Attorney, Agent or Firm: Klauber & Jackson Publication (No, Kind, Date), Applic (No, Date):

B1 20020820 US 99355160 19991001

Calculated Expiration: 20180127

Internat. Convention Pub (No, Date), Applic (No, Date): WO 9832864

19980730 WO 98GB244 19980127

Section 371: 19991001 Section 102(e):19991001

Priority Applic (No, Date): GB 971652 19970128

Abstract: The invention relates to a novel human class II PI3-kinase and in particular the sequence of the isolated nucleic acid molecule and the encoded amino acid sequence. The novel human PI3-kinase is termed PI3K-C2 alpha and has unique biochemical properties that characterize and distinguish it from known PI3-kinases. These include, amongst other things, resistance to the PI3-kinase inhibitors Wortmannin and LY294000, the lack of a p85 binding site, a divergent amino terminus and the absence of a polyproline motif which is typical of known type II PI3-kinases.

...Internat. Convention Pub(No,Date), Applic(No,Date): \*\*\*19980730\*\*\*

Exemplary Claim:

#### DRAWING

- \*\*\*1\*\*\* An isolated nucleic acid comprising: (a) a nucleotide sequence that encodes human PI3K-C2 alpha... Non-exemplary Claims:
- 2. The isolated nucleic acid of claim \*\*\*1\*\*\* wherein the nucleotide sequence is SEQ ID NO: \*\*\*1\*\*\* .
- ...3. The isolated nucleic acid of claim \*\*\*1\*\*\* which is a cDNA...
- ...4. An isolated nucleic acid that hybridizes to SEQ ID NO: \*\*\*1\*\*\* M \*\*\*sodium\*\*\* \*\*\*phosphate\*\*\* , pH 7.2, \*\*\*7\*\*\* % \*\*\*SDS\*\*\* \*\*\*1\*\*\* mΜ

EDTA at \*\*\*65\*\*\* degree(s) C. and remains bound after two washing steps with 0.5XSSC and 0. \*\*\*1\*\*\* % SDS for 20 minutes at 60 degree(s) C.; wherein the isolated nucleic acid encodes...

- ...a eukaryotic cell comprising: (a) an isolated nucleic acid that hybridizes to SEQ ID NO: \*\*\*1\*\*\* in 0.5 M \*\*\*sodium\*\*\* \*\*\*phosphate\*\*\*
- \*\*\*7\*\*\* % \*\*\*SDS\*\*\* , pH 7.2, \*\*\*1\*\*\* mM EDTA at degree(s) C. and

remains bound after two washing steps with 0.5XSSC and 0. \*\*\*1\*\*\* % SDS for 20 minutes at 60 degree(s) C.; wherein the isolated nucleic acid encodes

11/3,K,AB/2 (Item 2 from file: 340) DIALOG(R)File 340:CLAIMS(R)/US Patent (c) 2007 IFI/CLAIMS(R). All rts. reserv.

Dialog Acc No: 3416416 IFI Acc No: 0038035

IFI Publication Control No: 0038035

Document Type: C

RATH GENES AND POLYPEPTIDES AND METHODS FOR THE TREATMENT AND DIAGNOSIS OF IMMUNE DISORDERS; DETECTING NUCLEIC ACID INVOLVED IN G PROTEIN MEDIATED

SIGNAL TRANSDUCTION IN A T HELPER CELL SAMPLE

Inventors: Gimeno Carlos J (ÚS); Levinson Douglas Adam (US)

Assignee: Millennium Pharmaceuticals Inc

Assignee Code: 41994

Attorney, Agent or Firm: Pennie & Edmonds LLP Publication (No, Kind, Date), Applic (No, Date):

US 6146827 A 20001114 US 97949004 19971010

Calculated Expiration: 20161004

Cont.-in-part Pub(No), Applic(No, Date): US 5846780

96726228 19961004

Division Pub(No), Applic(No, Date): US 6020142

US 97870815

US

19970606

Priority Applic(No, Date): US 97949004 19971010; US 96726228

19961004; US 97870815 19970606

Abstract: The present invention relates, first, to the identification of novel nucleic acid molecules, termed RATH genes and RATH gene products encoded by such nucleic acid molecules, or degenerate variants thereof, that participate in the regulation, control and/or modulation of G-protein-mediated signal transduction involved in T cell activation, including, but not limited to T helper (TH) cell and TH cell subpopulation activation. Specifically, the nucleic acid molecules of the present invention include the genes corresponding to the mammalian RATH genes, including the RATH1. \*\*\*1\*\*\* genes. Sequence analysis indicates that the RATH genes are novel genes belonging to the RGS ("regulator of Gprotein signalling") gene family, a gene family which encodes gene products involved in G-protein-mediated signal transduction.

Publication (No,Kind,Date), Applic (No,Date):
... \*\*\*20001114\*\*\*

Abstract: ...the present invention include the genes corresponding to the mammalian RATH genes, including the RATH1. \*\*\*1\*\*\* genes. Sequence analysis indicates that the RATH genes are novel genes belonging to the RGS...

Exemplary Claim:

DRAWING

 $\star\star\star1\star\star\star$  . A method for detecting a RATH nucleic acid molecule in a T helper cell sample...

...encoded by the cDNA clone of ATCC Accession No. 98116 under conditions comprising incubation at \*\*\*65\*\*\* degree(s) C. in 0.5 M NaHPO4, \*\*\*7\*\*\* % \*\*\*SDS\*\*\* , \*\*\*1\*\*\* mM EDTA followed by washing in 0.1XSSC/0. \*\*\*1\*\*\* % SDS

at 68 degree(s) C. Non-exemplary Claims:

2. The method of claim \*\*\*1\*\*\* , wherein the reagent detects an mRNA molecule...

```
? s hybridization
     S1 438963 HYBRIDIZATION
? s 7(w)percent(w)SDS
        7153666 7
         533165 PERCENT
         135864 SDS
              0 7 (W) PERCENT (W) SDS
      S2
? s 7(1n)sds
        7153666 7
         135864 SDS
             622 7(1N)SDS
      S3
? s1 and s3
Processing
        15293543
                1
             622 S3
             501 1 AND S3
      S4
? s 65
      S5 585103 65
? s s4 and s5
             501 S4
          585103 S5
             103 S4 AND S5
      S6
? s sodium(w)phosphate
          920242 SODIUM
          501807 PHOSPHATE .
           15227 SODIUM (W) PHOSPHATE
      S7
? s s6 and s7
             103 S6
           15227 S7
              17 S6 AND S7
      S8
? rd
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>>>Records from unsupported files will be retained in the RD set.
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Processing
              17
                 S9
        40016186 PY<=2000
              4 S9 AND PY<=2000
     S10
? rd
>>>Duplicate detection is not supported for File 340.
>>>Records from unsupported files will be retained in the RD set.
               4 RD (unique items)
     S11
? t s11/3,k,ab/1-4
 11/3,K,AB/1
                (Item 1 from file: 340)
DIALOG(R) File 340: CLAIMS(R) /US Patent
(c) 2007 IFI/CLAIMS(R). All rts. reserv.
Dialog Acc No: 3736646 IFI Acc No: 0229010
IFI Publication Control No: 0229010
Document Type: C
LIPID KINASE; ISOLATED NUCLEIC ACID COMPRISING NUCLEOTIDE SEQUENCE THAT
ENCODES HUMAN PI3K-C2-ALPHA, A PHOSPHOINOSITIDE LIPID KINASE, HAVING
SPECIFIED AMINO ACID SEQUENCE
Inventors: Domin Jan (GB); Warerfield Michael Derek (GB)
Assignee: Ludwig Institute for Cancer Research CH
Assignee Code: 25199
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--**--**

Attorney, Agent or Firm: Klauber & Jackson Publication (No, Kind, Date), Applic (No, Date):

US 6436671 B1 20020820 US 99355160 19991001

Calculated Expiration: 20180127

Internat. Convention Pub (No, Date), Applic (No, Date): WO 9832864

19980730 WO 98GB244 19980127

Section 371: 19991001 Section 102(e):19991001

Priority Applic(No, Date): GB 971652 19970128

Abstract: The invention relates to a novel human class II PI3-kinase and in particular the sequence of the isolated nucleic acid molecule and the encoded amino acid sequence. The novel human PI3-kinase is termed PI3K-C2 alpha and has unique biochemical properties that characterize and distinguish it from known PI3-kinases. These include, amongst other things, resistance to the PI3-kinase inhibitors Wortmannin and LY294000, the lack of a p85 binding site, a divergent amino terminus and the absence of a polyproline motif which is typical of known type II PI3-kinases.

...Internat. Convention Pub(No,Date), Applic(No,Date): \*\*\*19980730\*\*\*

Exemplary Claim:

#### DRAWING

\*\*\*1\*\*\* . An isolated nucleic acid comprising: (a) a nucleotide sequence that encodes human PI3K-C2 alpha...
Non-exemplary Claims:

2. The isolated nucleic acid of claim \*\*\*1\*\*\* wherein the nucleotide sequence is SEQ ID NO: \*\*\*1\*\*\*

• •

```
PLEASE ENTER A COMMAND OR BE LOGGED OFF IN 5 MINUTES
? ds
Set
               Description
       Items
S1
       557004
               METASTA?
S2
         4975 (IN OR WITHIN) (5N) (PROSTATE (5N) TISSUE)
S3
          833
               S1 AND S2
          318
S4
               S3 AND PY<2000
S5
          166 RD (unique items)
S6
      1671325 LYMPH OR BONE OR SOFT
S7
          107
               S5 NOT S6
S8
          279·
               METAST? (5N) (PROSTATE (5N) TISSUE)
S9
          123
               S8 AND PY<=2000
S10
          67
               RD (unique items)
               IMAGING OR (SITU (5N) HYBRIDI?)
S11
      1312768
S12
          11
              S10 AND S11
? s metasta?(2n)(prostate(w)tissue)
          557004 METASTA?
          233105 PROSTATE
         2042278 TISSUE
             26 METASTA? (2N) (PROSTATE (W) TISSUE)
     S13
? rd
>>>Duplicate detection is not supported for File 340.
>>>Records from unsupported files will be retained in the RD set.
             11 RD (unique items)
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>>>Term "AMD" in invalid position
? s s14 and py<=2000
Processing
              11 S14
        40016186 PY<=2000
             5 S14 AND PY<=2000
? t s15/3, k, ab/1-5
```

(Item 1 from file: 155)

15/3,K,AB/1

DIALOG(R) File 155: MEDLINE(R)

Document Type: C

CANCER TREATMENTS; VACCINE COMPRISING COMBINATION OF THREE DIFFERENT CELL LINES LETHALLY IRRADIATED WITH GAMMA RADIATION TO ENSURE REPLICATION INCOMPETENCY

Inventors: Dalgleish Angus George (GB); Smith Peter Michael (GB); Sutton
Andrew Derek (GB); Walker Anthony Ian (GB)

Assignee: Onyvax Ltd GB Assignee Code: 66190

Attorney, Agent or Firm: Heller Ehrman White & McAuliffe

Publication (No, Kind, Date), Applic (No, Date):

US 6699483 B1 20040302 US 2001857690 20010907

Calculated Expiration: 20191209

Internat. Convention Pub(No, Date), Applic(No, Date): WO 200033870

20000615 WO 99GB4135 19991209

Section 371: 20010907 Section 102(e):20010907

Priority Applic (No, Date): GB 9827103 19981210

Abstract: The invention relates to a product comprised of specific combinations of cell lines intended for use as an allogeneic immunotherapy agent for the treatment of prostate cancer in humans. The heterogeneity of the immunotherapeutic matches the heterogeneity of the antigenic profile in the target prostate cancer and immunises the recipients with many of the potential TAA and TSA which are expressed at various stages of the disease. The invention discloses a vaccine comprising a combination of three different cell lines prepared from primary or metastatic prostate cancer biopsy material. The cell lines are lethally irradiated utilising gamma irradiation at 50-300 Gy to ensure that they are replication incompetent.

...Internat. Convention Pub(No,Date),Applic(No,Date): \*\*\*20000615\*\*\*
Non-exemplary Claims:

...derived from a primary prostate tumor and the other two cell lines are derived from \*\*\*metastatic\*\*\* \*\*\*prostate\*\*\* \*\*\*tissue\*\*\* .

...three different human prostate tumor cell lines, wherein one cell line is derived from a metastatic prostate tissue and the other two cell lines are derived from primary prostate turmors

05271319 Genuine Article#: VL878 Number of References: 21
Title: PRELIMINARY IMAGING RESULTS USING IN-111 LABELED CYT-356
(PROSTASCINT(TM)) IN THE DETECTION OF RECURRENT PROSTATE-CANCER
Abstract Available)

Author(s): SODEE DB; CONANT R; CHALFANT M; MIRON S; KLEIN E; BAHNSON R; SPIRNAK P; CARLIN B; BELLON EM; ROGERS B

Corporate Source: CASE WESTERN RESERVE UNIV, METROHLTH MED CTR, DEPT RADIOL, 2500 METROHLTH DR/CLEVELAND//OH/44109; CLEVELAND CLIN FDN, DEPT UROL ONCOL/CLEVELAND//OH/44195; UNIV PITTSBURGH, DEPT UROL/PITTSBURGH//PA/00000; CASE WESTERN RESERVE UNIV, METROHLTH MED CTR, DEPT UROL/CLEVELAND//OH/44109; CYTOGEN CORP/PRINCETON//NJ/00000

Journal: CLINICAL NUCLEAR MEDICINE, 1996, V21, N10 (OCT), P759-767

ISSN: 0363-9762

Language: ENGLISH Document Type: ARTICLE

Abstract: To evaluate whether In-111 capromab pendetide (an antibody conjugate directed to a glycoprotein found primarily on the cell membrane of prostate tissue) radioimmunoscintigraphy can localize residual or metastatic prostatic carcinoma in 15 patients after prostatectomy and lymphadenectomy for prostatic carcinoma with rising serum prostate-specific antigen. One patient with 0.6 ng/ml serum prostate-specific antigen had normal imaging results and 14 patients had scintigraphic evidence of residual prostatic bed or metastatic prostatic carcinoma. Two patients with borderline abnormal bone scans had abnormal activity in the same regions on In-111 capromab pendetide images. All patients had negative radiographic abdominal and pelvic cross-sectional prestudy images, and there were no adverse effects related to In-111 capromab pendetide infusion and little human antimouse antibody response.

Survey of gene amplifications during prostate cancer progression by high-throughput fluorescence in situ hybridization on tissue microarrays

AUTHOR: Bubendorf Lukas; Kononen Juha; Koivisto Pasi; Schraml Peter; Moch Holger; Gasser Thomas C; Willi Niels; Mihatsch Michael J; Sauter Guido; Kallioniemi Olli-P (Reprint)

AUTHOR ADDRESS: Cancer Genet. Branch, Natl. Human Genome Res. Inst., NIH, 49 Convent Dr., MSC 4470, Room 4A24, Bethesda, MD 20892-4470, USA\*\*USA JOURNAL: Cancer Research 59 (4): p803-806 Feb. 15, 1999 \*\*\*1999\*\*\*

MEDIUM: print ISSN: 0008-5472

DOCUMENT TYPE: Article RECORD TYPE: Abstract LANGUAGE: English

ABSTRACT: Prostate cancer development and progression is driven by the accumulation of genetic changes, the nature of which remains incompletely understood. To facilitate high-throughput analysis of molecular events taking place in primary, recurrent, and metastatic prostate \*\*\*tissue\*\*\* cancer, we constructed a microarray containing small 0.6-mm cylindrical samples acquired from 371 formalin-fixed blocks, including benign prostatic hyperplasia (n = 32) and primary tumors (n = 223), as well as both locally recurrent tumors (n = 54) and metastases (n = 62)from patients with hormone-refractory disease. Fluorescence in hybridization (FISH) was applied to the analysis of consecutive tissue microarray sections with probes for five different genes. High-level (gtoreq3X) amplifications were very rare (<2%) in primary prostate cancers. However, in metastases from patients with hormone-refractory disease, amplification of the androgen receptor gene was seen in 22%, MYC in 11%, and Cyclin-D1 in 5% of the cases. In specimens from locally recurrent tumors, the corresponding percentages were 23, 4, and 8%. ERBB2 and NMYC amplifications were never detected at any stage of prostate cancer progression. In conclusion, FISH to tissue microarray sections enables high-throughput analysis of genetic alterations contributing to cancer development and prog

Characterization of insulin-like growth factor-binding protein-related protein-1 in prostate cells.

Hwa V; Tomasini-Sprenger C; Bermejo A L; Rosenfeld R G; Plymate S R Department of Pediatrics, Oregon Health Sciences University, Portland 97201, USA:

Journal of clinical endocrinology and metabolism (UNITED STATES) Dec 1998, 83 (12) p4355-62, ISSN 0021-972X--Print Journal Code: 0375362

Contract/Grant Number: CA-58110; CA; NCI; DK-51513; DK; NIDDK; DK-52683; DK; NIDDK

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Insulin-like growth factor-binding protein-related protein-1 (IGFBP-rP1; also known as Mac25, TAF, and PSF) is a member of the IGFBP superfamily. It protein that shares structural and functional cysteine-rich \*\*\*situ\*\*\* with the conventional IGFBPs. Ιn similarities hybridization of prostate tissue sections show intense IGFBP-rP1 messenger ribonucleic acid (mRNA) expression in normal stroma and glandular epithelium. There was a significant loss of detectable IGFBP-rP1 mRNA in . IGFBP-rP1 mRNA \*\*\*tissue\*\*\* \*\*\*metastatic\*\*\* \*\*\*prostate\*\*\*

(Northern

blots) and protein (immunoblots) were detectable in primary cultures of prostatic stromal and epithelial cells as well as in the immortalized nonmalignant prostatic human epithelial cells, P69, and in the P69 metastatic subline, M12. IGFBP-rP1 expression was not detectable in the prostatic cancer cell lines PC-3, DU145, and LNCaP. IGFBP-rP1 expression was regulated in P69 cells but not in M12 cells. Protein and mRNA expression was up-regulated by IGF-I, transforming growth factor-beta, and retinoic acid. The observations that IGFBP-rP1 expression is significantly diminished in prostate tumorigenesis and is regulated in nonmalignant prostate cells suggest IGFBP-rP1 is important in normal prostatic cell

Glycotyping of prostate specific antigen.

Prakash S; Robbins P W

Center for Cancer Research, Massachusetts Institute of Technology, Cambridge, MA 02139, USA.

Glycobiology (ENGLAND) Feb 2000, 10 (2) p173-6, ISSN

0959-6658--Print Journal Code: 9104124

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Measurement of serum levels of the prostate specific antigen (PSA) is now widely used for the diagnosis of prostate cancer and benign prostate hyperplasia. This serum marker is of value since it is derived only from the tissue of interest, but increased levels of PSA in serum do not allow a completely clear cut diagnosis of benign versus malignant changes. Since PSA is a glycoprotein with one asparagine linked oligosaccharide, and since malignant transformation often leads to an increased branching of such oligosaccharides, we initially studied the asparagine linked structures on PSA made by a cell line derived from malignant metastatic

Glycotyping of prostate specific antigen.

Prakash S; Robbins P W

Center for Cancer Research, Massachusetts Institute of Technology,

Cambridge, MA 02139, USA.

Glycobiology (ENGLAND) Feb 2000, 10 (2) p173-6, ISSN

0959-6658--Print Journal Code: 9104124

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

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... \*\*\*2000\*\*\*

... studied the asparagine linked structures on PSA made by a cell line derived from malignant \*\*\*metastatic\*\*\* \*\*\*prostate\*\*\* \*\*\*tissue\*\*\*
. We observed that unlike normal PSA, which bears only biantennary oligosaccharides, PSA from the metastatic...

15/3,K,AB/2 (Item 2 from file:

Dialog Acc No: 2974655 IFI Acc No: 9813551 IFI Publication Control No: 9813551 Document Type: C PHOSPHOLIPASE D GENE ORIGINATED FROM PLANT; GENES AND CLONING DNA WITH NUCLEOTIDE SEQUENCES AND HYBRIDS Inventors: Morioka Shinji (JP); Ueki Jun (JP) Assignee: Japan Tobacco Inc JP Assignee Code: 43797 Attorney, Agent or Firm: Birch, Stewart, Kolasch & Birch LLP Publication (No, Kind, Date), Applic (No, Date): US 5747327 A 19980505 US 95446794 19950726 Calculated Expiration: 20150505 (Cited in 005 later patents) Internat. Convention Pub(No, Date), Applic(No, Date): WO 9509234 19950406 WO 94JP1627 19940930 Section 371: 19950726 Section 102(e):19950726 Priority Applic (No, Date): JP 93267884 19930930 Abstract: A cloned DNA encoding phospholipase D originated from a plant and a cloned DNA which regulates expression of phospholipase D gene originated from a plant are disclosed. Publication (No, Kind, Date), Applic (No, Date): \*\*\*19980505\*\*\* ...Internat. Convention Pub(No,Date), Applic(No,Date): \*\*\*19950406\*\*\* Exemplary Claim: \*\*\*1\*\*\* . A cloned DNA which encodes phospholipase D originated from a plant, wherein said DNA comprises... ... nucleotide sequence selected from the group consisting of nucleotides 182-2617 of SEQ ID NO:1 and nucleotides 107-2542 of SEQ ID NO:3 or a sequence complementary thereto or... ...to said cloned DNA or said complementary sequence in a hybridization solution containing 0.5M \*\*\*sodium\*\*\* \*\*\*phosphate\*\*\* buffer, pH 7.2, containing 7% SDS, 1 mM EDTA and 100 mg/ml of salmon sperm DNA at \*\*\*65\*\*\* \* C. for 16 hours and washing twice at \*\*\*65\*\*\* \* C. for twenty minutes in a washing solution containing 0.5 X SSC and 0. \*\*\*1\*\*\* % SDS. Non-exemplary Claims: 2. The DNA according to claim \*\*\*1\*\*\* , which encodes phospholipase D originated from a monocotyledonous plant... ...DNA according to claim 3, which has a nucleotide sequence shown in SEQ ID NO. \*\*\*1\*\*\* or has the same nucleotide sequence as shown in SEQ ID \*\*\*1\*\*\* except that one or more nucleotides are added, deleted or substituted, said nucleotide sequence encodes... ...DNA according to claim 7, which has a nucleotide sequence shown in SEQ ID NO. \*\*\*1\*\*\* ... sequence from 182th to 2617th nucleotide in the nucleotide sequence shown in SEQ ID NO. \*\*\*1\*\*\* ...DNA which has a nucleotide sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 3 and SEQ ID NO: 5 or a sequence

complementary thereto or...

- ...to said cloned DNA or said complementary sequence in a hybridization solution containing 0.5M \*\*\*sodium\*\*\* \*\*\*phosphate\*\*\* buffer, pH 7.2, containing 7% SDS, 1 mM EDTA and 100 Mu g/ml of salmon sperm DNA at 45\* C. or \*\*\*65\*\*\* \* C. for 16 hours and washing twice at 45\* C. or 650\* C. for twenty...
- ...mM sodium citrate or in a washing solution containing 0.5 X SSC containing 0. \*\*\*1\*\*\* % SDS...
- ...said DNA has a nucleotide sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 3 and SEQ ID NO: 5 or wherein said DNA specifically hybridizes to said antisense sequence in a hybridization solution containing 0.5M \*\*\*sodium\*\*\* \*\*\*phosphate\*\*\* buffer, pH 7.2, containing 7% SDS, 1 mM EDTA and 100 Mu g/ml of salmon sperm DNA, at 45\* C. or \*\*\*65\*\*\* \* C. for 16 hours and washing twice at 45\* C. or \*\*\*65\*\*\* \* C. for twenty minutes in a washing solution containing 0.3M NaCl and 30 mM sodium citrate or in a washing solution containing 0.5 X SSC containing 0. \*\*\*1\*\*\* % SDS

11/3,K,AB/4 (Item 4 from file: 340) DIALOG(R)File 340:CLAIMS(R)/US Patent (c) 2007 IFI/CLAIMS(R). All rts. reserv.

Dialog Acc No: 2241066 IFI Acc No: 9208761

IFI Publication Control No: 9208761

Document Type: C

INHIBIN ISOLATED FROM OVARIAN FOLLICULAR FLUID

Inventors: de Kretser David M (AU); Burger Henry G (AU); Findlay John K
(AU); Forage Robert G (AU); Hearn Milton T W (AU); Milne-Robertson

```
? s local?(ln)metasta?
         2165962 LOCAL?
           557046 METASTA?
       S1
            6407 LOCAL? (1N) METASTA?
 ? s recurren?
      S2 608112 RECURREN?
 ? s s1 not s2
             6407 S1
          608112 S2
       S3
            4075 S1 NOT S2
 ? s prostate (5n) tissue
          233127 PROSTATE
          2042487
                  TISSUE
            9441 PROSTATE (5N) TISSUE
       S4
 ? s s3 and s4
             4075 S3
             9441
                  S4
              25
                  S3 AND S4
       S5
? rd
 >>>Duplicate detection is not supported for File 340.
 >>>Records from unsupported files will be retained in the RD set.
              13 RD (unique items)
 ? s s6 and py<=2000
 Processing
 Processing
               13
                  S6
         40016443 PY<=2000
               4 S6 AND PY<=2000
 ? t s7/3,k,ab/1-4
                 (Item 1 from file: 155)
  7/3, K, AB/1
 DIALOG(R) File 155: MEDLINE(R)
 (c) format only 2007 Dialog. All rts. reserv.
 10989313
            PMID: 8806197
   Prostate cancer--biology of metastasis and its clinical implications.
   Dong J T; Rinker-Schaeffer C W; Ichikawa T; Barrett J C; Isaacs J T
   Johns Hopkins Oncology Center, Johns Hopkins University of School of
 Medicine, Baltimore, Maryland, USA.
   World journal of urology (GERMANY)
                                         1996,
                                                14
                                                   (3) p182-9,
 ISSN 0724-4983--Print
                         Journal Code: 8307716
   Publishing Model Print
   Document type: Journal Article; Review
   Languages: ENGLISH
   Main Citation Owner: NLM
   Record type: MEDLINE; Completed
   Prostate cancer is one of the most commonly diagnosed cancers and is a
 major cause of cancer death in men. Although the majority of the diagnosed
 prostate cancers will remain localized and never produce clinical symptoms
 during the lifetime of the host, a subset of these cancers will progress to
 a more malignant state requiring therapeutic intervention. Acquisition of
 metastatic ability by prostatic cancer cells is the most lethal aspect of
 prostatic cancer progression. Once this has occurred, definitive therapy is
 required before the initially localized metastatic cells escape
 from the prostate. At present, metastatic prostate cancer is incurable.
 Therefore, there is an urgent need to develop molecular markers that can be
 used to predict the metastatic potential of prostate cancers. Using somatic
 cell hybridization, we have demonstrated that acquisition of metastatic
 ability requires both the loss of metastasis-suppressor function(s) and the
```

activation of oncogenes. In further studies using micro-cell-mediated

chromosomal transfer, we located genes on human chromosome, 8, 10cen-q23, 11p11.2-13, and 17pter-q23, which, when introduced into rat prostatic cancer cells, are capable of suppressing their metastatic ability without affecting their tumorigenicity or growth rate in vivo. Initially we focused upon the human chromosome 11p11.2-13 region to clone metastasis-suppressor gene(s) positionally. One such gene, termed KAI-1, encodes a membrane glycoprotein. KAI-1 has been mapped to the p11.2 region of human chromosome 11 by fluorescence in-situ hybridization analysis. Expression of KAI-1 has been detected in all normal human tissues thus far tested, including \*\*\*prostate\*\*\* \*\*\*tissue\*\*\* . When introduced into rat metastatic prostatic cancer cells, KAI-1 significantly suppressed the metastasis without affecting the tumor growth rate. KAI-1 expression is high in human normal prostate and benign prostatic hyperplasia but is dramatically lower in cancer cell lines derived from metastatic prostate tumors.

... \*\*\*1996\*\*\*

... of prostatic cancer progression. Once this has occurred, definitive therapy is required before the initially localized metastatic cells escape from the prostate. At present, metastatic prostate cancer is incurable. Therefore, there is...

... of KAI-1 has been detected in all normal human tissues thus far tested, including \*\*\*prostate\*\*\* \*\*\*tissue\*\*\* . When introduced into rat metastatic prostatic cancer cells, KAI-1 significantly suppressed the metastasis without...

7/3,K,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2007 Dialog. All rts. reserv.

07300915 PMID: 3828960

Relationship between androgen receptor binding activity in human prostate cancer and clinical response to endocrine therapy.

Benson R C; Gorman P A; O'Brien P C; Holicky E L; Veneziale C M Cancer (UNITED STATES) May 1 1987, 59 (9) p1599-606, ISSN 0008-543X--Print Journal Code: 0374236

Publishing Model Print

Expression of the cellular adhesion molecule E-cadherin is reduced or absent in high-grade prostate cancer.

Umbas R; Schalken J A; Aalders T W; Carter B S; Karthaus H F; Schaafsma H E; Debruyne F M; Isaacs W B

Department of Urology/Urological Research Laboratories, University Hospital, Nijmegen, The Netherlands.

Cancer research (UNITED STATES) Sep 15 1992, 52 (18) p5104-9,

ISSN 0008-5472--Print Journal Code: 2984705R

Contract/Grant No.: CA5523101; CA; NCI

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

E-cadherin is a Ca(2+)-dependent cell adhesion molecule which plays an important role in normal growth and development via mediation of homotypic, homophilic cell-cell interaction. Recent studies suggest that E-cadherin may be important in neoplastic progression as well, particularly as a suppressor of invasion. We have previously demonstrated that the invasive phenotype of rat prostate cancer cells is associated with the decreased expression of E-cadherin (M. J. G. Bussemakers, R. J. A. Van Moorselaar, L. A. Giroldi, T. Ichikawa, J. T. Isaacs, F. M. J. Debruyne, and J. A. Schalken, Cancer Res., 52:2916-2922, 1992). This is of particular interest, since the locus to which the human E-cadherin gene is mapped is frequently involved in allelic loss in prostate cancer (B. S. Carter, C. M. Ewing, W. S. Ward, B. F. Treiger, T. W. Aalders, J. A. Schalken, J. I. Epstein, and W. B. Isaacs, Proc. Natl. Acad. Sci. USA, 87:8751-8755, 1990; U. S. Bergerheim, K. Kunimi, V. P. Collins, and P. Ekman, Genes, Chromosomes Cancer, 3: 215-220, 1991). Impaired E-cadherin function is likely to be associated with aberrant expression of the protein. We therefore analyzed E-cadherin expression in situ by immunohistochemistry in nonmalignant and malignant specimens of human prostatic tissue. Of 92 tumor samples of either primary or metastatic deposits of prostate cancer, 46 had or absent E-cadherin staining when compared to nomalignant prostate, which uniformly stained strongly positive. There was a statistically significant correlation between the decreased expression of E-cadherin and loss of tumor differentiation. Additionally, certain tumors within a histologically similar group could be distinguished by the presence of mixed populations of E-cadherin-negative and -positive cells. The percentage of tumors with aberrant E-cadherin staining increased when clinically localized tumors were compared to either tumors with extensive local progression or metastatic deposits of prostate cancer, suggesting a correlation between loss of E-cadherin and tumor progression. Taken together, these findings suggest that further exploration of E-cadherin as a candidate invasion suppressor molecule in human prostate cancer is warranted.

## ... \*\*\*1992\*\*\*

...to be associated with aberrant expression of the protein. We therefore analyzed E-cadherin expression in situ by immunohistochemistry in nonmalignant and malignant specimens of human prostatic tissue. Of 92 tumor samples...

... E-cadherin staining increased when clinically localized tumors were compared to either tumors with extensive local progression or metastatic deposits of prostate cancer, suggesting a correlation between loss of E-cadherin and tumor progression. Taken together, these findings...

7/3,K,AB/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2007 Dialog. All rts. reserv.

09127646 PMID: 1823040

Superficial bladder cancer: survival and prognostic factors.

Sanchez de la Muela P; Rosell D; Aguera L; De Castro F; Isa W; Robles J E

; Zudaire J J; Berian J M

Department of Urology, University Hospital, Navarra University, Pamplona, Spain.

European urology (SWITZERLAND) 1991, 20 (3) p184-91, ISSN

0302-2838--Print Journal Code: 7512719

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Trisomy 7: a potential cytogenetic marker of human prostate cancer
 \*\*\*progression\*\*\* .

Bandyk M G; Zhao L; Troncoso P; Pisters L L; Palmer J L; von Eschenbach A C; Chung L W; Liang J C

Department of Urology, University of Texas M.D. Anderson Cancer Center, Houston 77030.

Genes, chromosomes & cancer (UNITED STATES) Jan 1994, 9 (1) p19-27, ISSN 1045-2257--Print Journal Code: 9007329

Contract/Grant No.: CA-56307; CA; NCI; RO1-CA43585; CA; NCI

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

We used the fluorescence in situ hybridization (FISH) method to show that chromosome 7 trisomy is associated with the progression \*\*\*cancer\*\*\* . Thirty-six specimens including 15 primary of human prostate prostate carcinomas, 16 metastatic lesions, and 5 normal prostate tissues, as well as 2 prostate carcinoma cell lines of different tumorigenic potential, were examined for chromosome 7 aneuploidy. Our results showed that the androgen-unresponsive tumorigenic cell line PC-3 exhibited a significantly higher ratio of chromosome 7 to total chromosome number than the androgen-responsive nontumorigenic cell line LNCaP (P=0.001). In prostate specimens, the frequency of trisomy 7 cells was significantly increased (P < 0.05) in the advanced stage tumors (C and DI) but not in the early (B) stage tumors or normal prostatic tissue. Furthermore, metastases showed a higher frequency of trisomy 7 cells than primary tumors (P =0.005). In 2 patients with paired primary and metastatic tumors, trisomy 7 cells increased from 4-7% in the primary tumors to 42-45% in the metastatic tumor cells in the bone marrow. Therefore, our data suggest that trisomy 7 may be a common feature associated with local and metastatic progression and serve as a novel marker for human prostate cancer \*\*\*progression\*\*\*

Trisomy 7: a potential cytogenetic marker of human p